Clinical effects of the exposure to red wine during at-home bleaching

Lucas Lage Menezes, DDS, MS/Suellen Nogueira Linares Lima, DDS, MS/Etevaldo Matos Maia-Filho, DDS, MS, PhD/Elizabeth Soares Fernandes, PhD/Saulo Jose Figueredo Mendes, PhD/Leticia Machado Gonçalves, DDS, MS, PhD/Matheus Coelho Bandeca, DDS, MS, PhD/Alessandra Reis, DDS, MS, PhD/Alessandro D. Loguercio, DDS, MS, PhD/Rudys Rodolfo De Jesus Tavarez, DDS, MS, PhD

Objectives: This clinical trial evaluated the effects of red wine exposure on the effectiveness of at-home bleaching with 10% carbamide peroxide, degree of tooth sensitivity, and levels of periodontal inflammatory markers. **Method and materials:** Eighty participants were assigned to two groups, namely, those who drank red wine (experimental group), and those who did not drink red wine (control group). The experimental group participants rinsed their mouths with 25 mL of red wine four times a day during the bleaching period. Shade evaluation was assessed visually by using the Vita Classical and Vita Easyshade techniques. Tooth sensitivity was evaluated by the numeric and visual analog scales, and the salivary and gingival crevicular fluids were collected for assessment of nitric oxide (NO) levels, a marker of inflammation. Differences in color change were analyzed by one-way analysis of variance (ANOVA). The absolute risks of tooth sensitivity were compared by the Fisher exact test. Tooth sensitivity intensity data sets for both the visual analog scale and the numeric rating scale were compared using the Wilcoxon signed rank test ($\alpha = .05$). Repeated measures and two-way ANOVA followed by the Bonferroni test were used to assess time-course and differences between groups in NO production. **Results:** The bleaching technique was effective regardless of wine consumption ($P > .05$). Tooth sensitivity was classified as mild, with no differences between groups ($P > .05$). Red wine reduced both the gingival crevicular fluid and salivary levels of NO ($P < .05$). **Conclusion:** Red wine does not interfere with the effectiveness and sensitivity of at-home teeth bleaching with 10% carbamide peroxide and protects against bleaching-induced inflammation. *(Quintessence Int 2022;53:48–57; doi: 10.3290/j.qi.b1864313)*

Key words: at-home bleaching, carbamide peroxide, crevicular gingival fluid, nitric oxide, tooth sensitivity

Among all available options of cosmetic procedures in dentistry, dental bleaching is certainly the most sought-after procedure. It can be done at home by using low-concentrated hydrogen peroxide (H_2O_2) or carbamide peroxide gels, or in the office using higher concentrations of these bleaching agents.[1]

Regardless of the bleaching protocol employed, clinicians often ask patients to stop drinking coffee, red wine, coke, or any type of pigmented foods and beverages. This caution has been taken as some in vitro studies have suggested that the concomitant exposure of this colored diet may jeopardize bleaching efficacy.[2-5] On the other hand, the available clinical trials do not support this hypothesis. Indeed, it was shown that exposure to coffee and tea during bleaching does not have a negative impact on color change.[6,7] Also, the consumption of coke during in-office bleaching treatment did not affect color change[8]; hence, pigment-containing diets may not have any detrimental effects on color change.[9]

However, it is uncertain if other types of colored diet components can affect bleaching results. Red wine is an acidic drink largely consumed worldwide. It gained popularity after the identification of anti-inflammatory and antioxidant compounds, such as polyphenols, in its composition.[10] These are suggested to pro-

tect against cardiovascular and inflammatory bowel diseases.[11,12] Red wine extracts were also found to have antimicrobial activities against periodontal pathogens[13] and to decrease macrophage-mediated inflammatory responses.[14,15] Interestingly, it was demonstrated that tooth bleaching agents can induce crevicular inflammation and damage, a response largely associated with nitric oxide (NO) synthesis and leukocyte activation.[16]

Therefore, this clinical trial aimed to investigate whether red wine exposure affects the effectiveness of bleaching with 10% carbamide peroxide, as well as the degree of tooth sensitivity (TS) and periodontal inflammation.

Method and materials

Ethics approval and protocol registration

The study protocol was conducted in full accordance with the World Medical Association Declaration of Helsinki, approved by the Committee for the Protection of Human Participants of the local university (protocol number: 2.271.693), and registered in the Brazilian Clinical Trials Registry (REBEC number RBR-3x9m5j). The report of this study followed the Consolidated Standards of Reporting Trials (CONSORT) statement.[17]

Trial design, settings, and locations of data collection

This study was a controlled trial with a parallel design in which the evaluator was masked to group assignments. All participants were informed about the nature and objectives of the study. The study was performed from October 2018 to June 2019 in the Clinics of the School of Dentistry from the State University of Ponta Grossa, PR, Brazil.

Recruitment

Recruitment was performed by posting written advertisements on the university walls. All volunteers signed an informed consent form before being enrolled in the study.

Eligibility criteria

Participants were 18 to 40 years old and presented with good general and oral health (without need of restorative, periodontal, endodontic, and surgical treatments). Participants were required to have anterior teeth without cavities, restorations, or periodontal disease, and maxillary incisors of shade A2 or darker as determined by the Vita Classical Shade Guide (VITA Zahnfabrik).

Pregnant or lactating women, smokers, and participants suffering from bruxism were excluded from the study. Participants with poor oral hygiene, who had undergone teeth-whitening treatment, with maxillary anterior teeth with endodontic treatment, visible enamel cracks, gingival recessions, cervical lesions or fractures, spontaneous TS, severe internal discoloration, and used fixed orthodontic appliances were also excluded from the study.

Sample size calculation

The primary outcome of this study was bleaching efficacy. A whitening degree (ΔE, CIEL*a*b*, 1978)[18] of approximately 7.4 ± 3.0 was previously observed for a 10% carbamide peroxide gel.[19,20] Thus, a minimal sample size of 32 participants per group was required to have a 90% chance of detecting an equivalence limit of 2.5 units between the control and experimental groups. The equivalence limit was determined by the 50:50% acceptability limit for ΔE_{76}.[21] Finally, 30% more patients were added to compensate for any dropout.

Sequence generation and allocation concealment

Patients who met the inclusion criteria were asked about their daily wine consumption. Those who did not drink wine were allocated to the control group. No other dietary restrictions were placed on the participants in the control group. The participants that reported drinking wine were placed in the experimental group. Participants in both groups were instructed not to eat pigmented foods or drinks such as coffee, soft drinks, red sauces, grape juice, and beets, in order to produce a better scenario to evaluate only the effect of wine. To ensure that this recommendation was followed, the patients filled a diet diary, in which they reported all food consumption.

Blinding

This was evaluator-blind (SNLL) for the clinical trial, and evaluator-blind (SJFM) for levels of periodontal inflammatory markers, but the patient and operator (LLM) were not masked to the group assignments. However, the evaluator who assessed color changes throughout the bleaching protocol was blinded to the group assignments.

Study intervention

A total of 80 participants were divided in to two groups (control, n = 40, and experimental, n = 40). Alginate impressions of

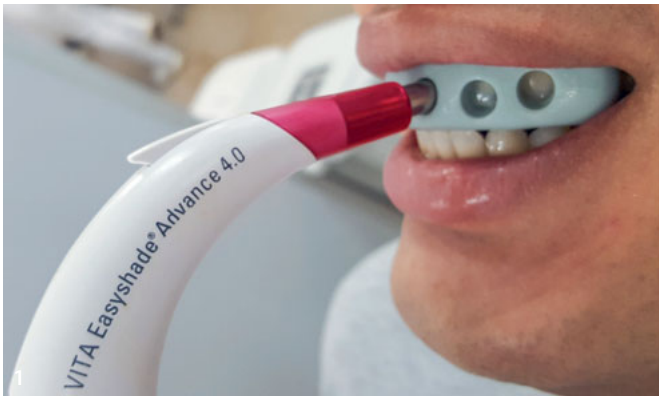


Fig 1 Silicone guide with the tip of the Vita Easyshade spectrophotometer to standardize color selection.

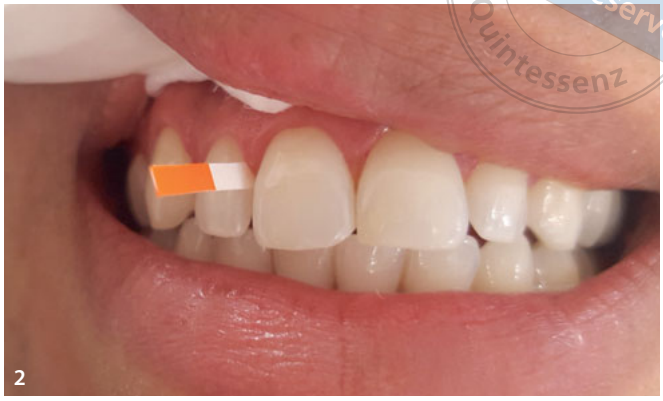


Fig 2 Strip inserted in the groove at a depth of 1–2 mm to collect gingival crevicular fluid.

each subject's maxillary and mandibular arch were made and these were filled with dental stone. No block-out material was applied to the labial surfaces of the stone model teeth. A 1-mm soft vinyl material provided by the manufacturer (FGM Dental Products) was used to make custom-fitted bleaching trays, which were trimmed 1-mm beyond the gingival margin.

Participants in the control group performed dentist-supervised at-home dental bleaching with 10% carbamide peroxide (Whiteness Perfect, FGM) for 4 hours daily for 3 weeks. All patients used the tray during the day (in the morning or in the afternoon) to guarantee that the bleaching procedure was not interrupted.

The experimental group consisted of subjects who reported drinking at least one bottle of red wine per week and were considered moderate consumers.[22] They were subjected to the same bleaching procedure and were asked to rinse their mouths with 25 mL of red wine (Grand Expedition Merlot, Bento Gonçalves, 11.5% vol.) for 30 seconds four times a day, at approximately 4-hour intervals.

Measurement of the study outcomes

Primary outcome: color change

Color changes were assessed by the subjective method Vita Classical (Vita Zahnfabrik), and objectively by Vita Easyshade spectrophotometry (Vident) at baseline, once a week for the first 3 weeks of bleaching, and 4 weeks after the end of the bleaching procedure. The Vita Classical scale was arranged in 16 tabs from the highest (B1) to the lowest (C4) values: B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, and C4. Although this scale is not linear, color changes were considered as continuous and linear variables as performed in previous controlled trials.[23] Color changes were calculated from the start of the active phase to each individual time-point assessed by calculating the change in the number of shade guide units (ΔSGU) that occurred towards the lighter end of the value-oriented list of shade-tabs.

For the Vita Easyshade spectrophotometry, an impression of the maxillary incisors was taken with dense silicone (Coltoflax and Perfil Cub Kit, Vigodent) and a 6-mm window was created in the middle third area of the maxillary right central incisor (Fig 1). The tip of the Vita Easyshade spectrophotometer device was then inserted into the silicone guide and the L*, a*, and b* parameters of color were obtained from the CIELab space. The L* value represents the luminosity (value from 0 [black] to 100 [white]), a* value represents the measurement along the red-green axis, and b* value represents the measurement along the yellow-blue axis. The color change (ΔE) before (baseline) and after each assessment period was calculated using the following CIELab formula: $\Delta E = [(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2]^{1/2}$.

Before start the color measures of each patient, the Vita Easyshade system was always calibrated. One calibrated evaluator recorded the color of each patient's teeth at baseline and at all experimental time-points. In case of disagreements, they were asked to reach a consensus before the patient was dismissed.

Secondary outcomes

Tooth sensitivity evaluation

Participants were asked to keep a daily record of whether they experienced sensitivity. They were instructed to register imme-

diately after the occurrence of TS. For this purpose the five-point verbal numeric rating scale (NRS) and the visual analog scale (VAS) were used at all evaluation times. The NRS comprises the following criteria:

- 0 = none
- 1 = mild
- 2 = moderate
- 3 = considerable
- 4 = severe.

The VAS scale employs a 10-cm horizontal line with the words "no pain" at one end and "worst pain" at the opposite end. The length in mm from the marked point to the zero end (no pain) was measured with a millimeter ruler, and allowed us to determine pain thresholds and it was used as index of TS intensity during treatment.

If the participant scored 0 (no sensitivity) at all time points, this subject was considered to be insensitive to the bleaching protocol. In all other circumstances, the participants were considered to have bleaching-induced TS. This dichotomization allowed us to calculate the absolute risk of TS, which is the percentage of patients who reported TS at least once during treatment.

Collection of gingival crevicular fluid and saliva samples

Gingival crevicular fluid (GCF) samples were collected (at baseline and different time-points following bleaching) as described by Lima et al.[24] Following isolation, teeth were air-dried. Samples were then, randomly collected from three maxillary sites per patient with a standard paper strip (Perio-paper; IDE Interstate). The strips were inserted in the sulcus to the depth of 1 to 2 mm for 15 seconds (Fig 2). After removal, blood-free strips (01 from each tooth) were placed in to Eppendorf tubes and kept at −80°C for further analysis. In parallel, non-stimulated salivary samples were collected in a 15-mL tube for 5 minutes. Then, samples were centrifuged at 2,000 rpm for 10 minutes and the supernatant was collected and kept at −80°C for analysis.

Nitric oxide (NO) levels

On the day of analysis, the strips containing GCF were eluted in 200 µL of sterile phosphate-buffered saline (PBS), vortexed, and centrifuged at 10,000 rpm for 10 minutes. The strips were discarded and the resulting samples were used in the assay. NO^{3-} content was reduced to NO^{2-} by incubating 80 µL of each saliva and GCF sample with 20 µL of 1 U/mL nitrate reductase (Sigma-Aldrich) and 10 µL of 1 mol/L NADPH (Sigma-Aldrich) for 30 minutes at 37°C.[25] Then, 100 µL of Griess reagent (5% v/v H_3PO_4 containing 1% w/v sulfanilic acid and 0.1% w/v N-1-napthylethylenediamine; Sigma-Aldrich) and samples were incubated for another 30 minutes at 37°C. Absorbance was read at 550 nm. The absorbance of each sample was subtracted by the blank sample absorbance and compared against a standard curve (0 to 300 µmol/L sodium nitrite) and expressed as NO levels in µmol/L.

Statistical analysis

The analysis followed the intent-to-treat protocol and involved all participants, who were divided in two groups. Two one-sided *t* tests for independent samples (TOST) were used to test the equivalence of the study groups at the different assessment points (baseline vs 1 week, baseline vs 2 weeks, baseline vs 3 weeks, and baseline vs 1 month post-bleaching).

Such an approach includes a right-sided test for the lower margin of the equivalence limit and a left-sided test for the upper margin using one-sided .025 significance levels. The overall *P* value is considered to be the larger of the two *P* values obtained from the lower and upper tests. A *P* value lower than the critical .05 significant level meant that equivalence could be claimed. Mean difference and 95% confidence interval (CI) were calculated between groups at each time assessment.

For ΔE, if both treatments differed by more than 2.5 units in either direction, then equivalence would not hold. Although not powered for, equivalence was similarly evaluated for color change in SGU (defined as a change in 1.0 SGU). A traditional repeated-measures one-way ANOVA was employed for each color change instrument to detect color changes over time.

The absolute risks of TS of both groups were compared by means of Fisher exact test. The relative risk as well as the CI for the effect size was also calculated. The TS intensity data set for both the VAS and NRS scales were plotted in histograms and inspected for normal distributions. As data did not have normal distribution, the groups were compared using the Wilcoxon signed rank test (α = .05) at each time assessment. The statistical program used for statistical analysis was SPSS 23.0 (IBM). Finally, repeated-measures and two-way ANOVA followed by the Bonferroni test was used for analysis of effects on NO levels.

Results

Characteristics of included participants

A total of 113 participants were examined according to the inclusion and exclusion criteria, but only 80 participants remained for the clinical trial. The reasons for exclusion are described in Fig 3. All participants attended the follow-up visits

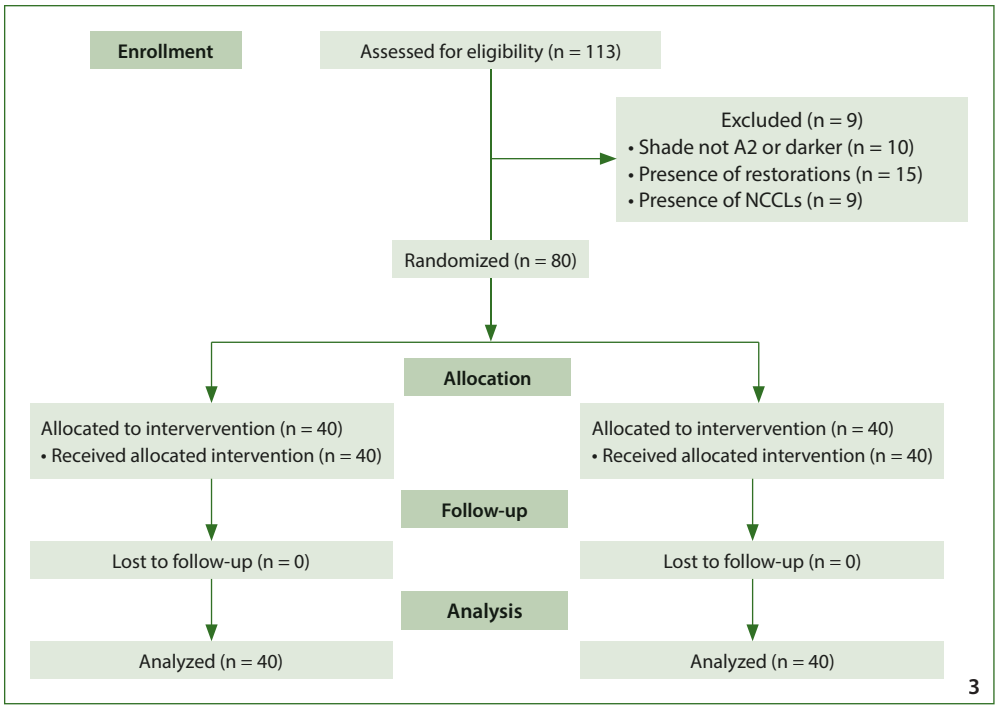


Fig 3 Flow chart of the different phases of the study. NCCL, non-carious cervical lesion.

Table 1 Characteristics of participants

Characteristic	Control	Experimental
Age (years; mean ± SD)	24.8 ± 6.0	26.4 ± 5.4
Baseline color (SGU; mean ± SD)*	8.3 ± 3.0	8.2 ± 2.4

*Vita Classical (Vita Zahnfabrik).

during the bleaching protocol and none quit the treatment. Usually, the dietary recommendation was followed for the majority of patients. Figure 3 depicts the participant flow diagram in the different phases of the study design. The initial tooth colors of both groups was assessed by the Vita Classical Shade Guide (VITA Zahnfabrik). Baseline measures were of 8.3 ± 3.0 and 8.2 ± 2.4 SGU (mean ± standard deviation [SD]), for the control and experimental groups, respectively. The mean age was around 25 years old (Table 1).

Color change

The means and SDs of color change in ΔSGU and ΔE for the control and experimental groups are presented in Table 2. In both groups, a whitening of approximately 9.5 units of ΔE and 7.0 units of ΔSGU ($P < .05$) at the end of the treatment was observed. Equivalence was claimed in most of the time-points assessed, except for ΔSGU obtained after the first week of bleaching.

Tooth sensitivity

Table 3 shows the absolute and relative risk of TS during the bleaching protocol for both groups. Most of the participants, above 92%, from both groups experienced TS at least once during the study. No significant differences between groups were detected (Fisher test, P value > .05).

The mean and SD values of TS in both pain scales (NRS and VAS) at the different assessment times are depicted in Table 4. No significant differences between groups were observed at any time-points ($P > .05$).

Nitric oxide (NO) levels

Data depicted in Fig 4 demonstrate the salivary and GCF levels of NO of patients undergoing tooth bleaching. Prior to bleaching, all subjects exhibited similar GCF and salivary levels of NO (Fig 4). A significant increase of NO was observed for GCF samples of control patients at the first week of bleaching (Fig 4a; $P < .05$). The same subjects exhibited elevated levels of salivary NO from the second week of bleaching (Fig 4b; $P < .05$). The sal-

Table 2 Color change in ΔE and ΔSGU (means, SDs, and mean difference) for both groups and the lowest *P* value from the two TOST statistics

Color instrument	Time assessment	Experimental	Control	Mean difference (95% CI)	Greater of the two one-sided *P* values	Equivalent?
ΔSGU Vita classical	Baseline vs. 1 week	4.8 ± 2.2	3.9 ± 1.9	0.9 (−0.02 to 1.82)	.436	No
	Baseline vs. 2 weeks	6.1 ± 2.2	6.1 ± 2.2	0.0 (−0.82 to 0.82)	.02	Yes
	Baseline vs. 3 weeks	7.0 ± 2.4	6.9 ± 2.7	0.05 (−0.9 to 1.0)	.05	Yes
	Baseline vs. 4 weeks post-bleaching	7.0 ± 2.4	7.0 ± 2.7	0.03 (−0.92 to 0.97)	.046	Yes
ΔE	Baseline vs. 1 week	6.0 ± 3.2	5.8 ± 3.3	0.2 (−0.98 to 1.4)	.001	Yes
	Baseline vs. 2 weeks	8.4 ± 3.7	8.3 ± 3.6	0.13 (−1.2 to 1.5)	.002	Yes
	Baseline vs. 3 weeks	9.8 ± 4.6	10.0 ± 4.1	−0.2 (− 1.8 to 1.4)	.01	Yes
	Baseline vs. 4 weeks post-bleaching	8.9 ± 4.6	9.9 ± 4.5	−1.0 (−2.5. to 0.62)	.049	Yes

Table 3 Absolute and relative risk of tooth sensitivity during bleaching

Group	Number of patients with TS	Absolute risk of TS (95% CI)	Relative risk of TS (95% CI)
Experimental (n = 40)	37	92.5 (80.1 to 97.4)	0.94 (0.85 to 1.04)
Control (n = 40)	39	97.5 (87.1 to 99.5)	

Fisher test; *P* value = .615

Table 4 Sensitivity values in the NRS and VAS scales according to the time of evaluation

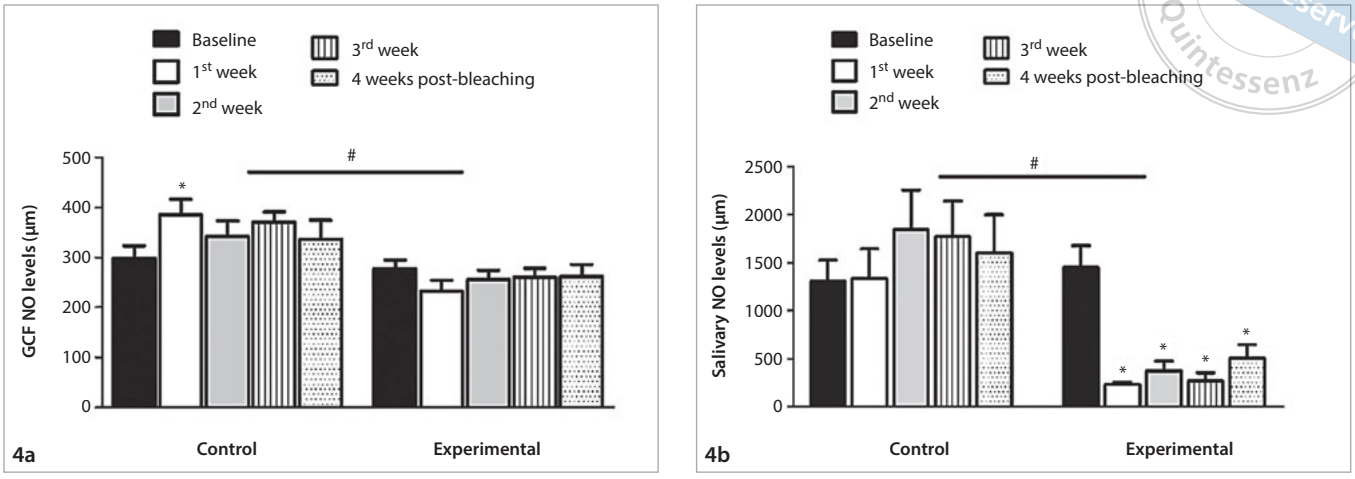
Color instrument	Time assessment	Experimental	Control	Mean difference (95% CI)	*P* value
NRS	During 1st week	1.1 ± 0.8	1.1 ± 0.9	0.0 (−0.4 to 0.4)	.833
	During 2nd week	1.1 ± 0.8	1.2 ± 1.0	0.0 (−0.4 to 0.4)	.775
	During 3rd week	1.1 ± 0.8	1.4 ± 1.0	0.3 (−0.1 to 0.7)	.151
VAS 0–10	During 1st week	1.3 ± 1.4	1.4 ± 2.1	0.1 (−0.7 to 0.9)	.732
	During 2nd week	1.3 ± 1.4	1.3 ± 1.5	0.0 (−0.7 to 0.7)	.768
	During 3rd week	1.2 ± 1.3	1.6 ± 1.8	0.4 (−0.3 to 1.1)	.598

ivary levels of NO remained elevated in these individuals at 4 weeks post-bleaching (Fig 4b; $P < .05$). On the other hand, those who rinsed their mouths with red wine presented with attenuated NO production at both crevicular and salivary sites (Fig 4; $P > .05$).

Discussion

Pigments like anthocyanins, present in the skin of grapes, which give red wine its dusky red color, can easily bind to the dental structure of some patients. The reddish appearance of teeth following red wine consumption is a matter of concern for some people. This can be verified through a simple Google search, which yields several tips to avoid this particular form of dental staining. In line with this concern, there are wine wipes available on the market, which claim to wipe wine stains off of the teeth without interfering with the wine's taste.

This concern is especially relevant for patients who undergo tooth bleaching. Alterations in tooth enamel occur during bleaching due to the acidic nature of the great majority of bleaching agents on the market for this procedure.[26] Demineralization is an expected enamel alteration after bleach-



Figs 4a and 4b Effects of wine rinse on the gingival crevicular fluid (GCF) and salivary nitric oxide (NO) levels in individuals undergoing bleaching with carbamide peroxide. NO levels in *(a)* GCF and *(b)* salivary samples of individuals undergoing carbamide peroxide. Wine (25 mL) was rinsed four times a day for 30 s, with intervals of approximately 4 hr between each rinse. $^{*}P < .05$, differs from baseline; $^{\#}P < .05$, differs from the control group.

ing, which could make the substrate more susceptible to staining by wine.[10]

Some interesting alternatives have been evaluated to decrease enamel demineralization or even help improve the remineralization process. For instance, laser irradiation, either alone or in combination with fluoride, causes a significant increase in enamel erosion resistance.[27,28] Further, Zirk et al[29] observed a higher potential of remineralization of artificial enamel caries lesions when applied to novel nanoscaled metal fluorides with relatively low free fluoride concentrations. Therefore, future studies should evaluate the potential of alternative therapies, such as laser irradiation and nanoscaled metal fluorides, to decrease enamel demineralization due to tooth bleaching, or even help improve the remineralization process.

However, the present investigation showed equivalent color changes after bleaching, both in those who did and did not rinse their mouths with red wine. Nonetheless, the extrinsic staining potential of red wine on the dental surface cannot be denied, as reported earlier, although it should be noted that this is temporary and easily reversible by the effect of saliva.[10] In this context, it is worth stating that saliva is able to reverse tooth demineralization by replacing the minerals lost during bleaching.[30] This is proven to be somewhat true when in vitro and in situ studies that evaluated morphologic alterations after at-home bleaching are compared. While in vitro studies showed some demineralization pattern or enamel microhardness reduction, this was not observed in in situ studies. Additionally, when contact between teeth and saliva occurs during all at-home bleaching procedures, no significant problems in terms of demineralization are observed.[31,32]

It is also important to mention that the pigments present in coffee, wine, and other colored drinks and foods are composed of macromolecular chains that cannot easily penetrate the dental structure within the short period of time they are in contact with the enamel during the bleaching protocol.[33] Similarly, an equivalent color change was observed for smokers and nonsmokers undergoing tooth bleaching.[34]

TS is one of the main adverse effects of tooth whitening and may be responsible for patients' discontinuation of the procedure.[35] Findings from previous studies[36-38] indicate that the mechanisms that lead to TS are not fully established, although it is believed that they are associated with bleaching-induced permeability of the enamel and dentin, which allows the chemical to penetrate the dental structure, causing sensitization of the nerve endings present in the dentin, resulting in discomfort to the patient.[32]

Other studies[39,40] have also correlated TS with the concentration of the bleaching product used, with reports demonstrating higher levels of sensitivity during in-office bleaching than at-home bleaching; however, it is not uncommon for sensitivity to be related to patients' pain threshold and not only the concentration of the product.[39]

In the present study, it was observed that approximately 92% of patients presented TS at some point during the bleaching procedure. This finding corroborates the literature that suggests a considerable proportion of patients experience sensitivity during and after the bleaching treatment.[23,41,42] It should be noted that bleaching-induced TS is transitory, and this may be due to the continuous presence and protective effects of saliva, as well as the correct dosage of the product, which both ensure the conservation of the characteristics of the surface of the dental enamel and promote its constant remineralization.[31]

Findings also revealed that H_2O_2-based tooth bleaching agents are suggested to cause tissue damage, a response that was associated with reduction of GCF NO levels from days 1 to 7 following bleaching.[16] In the present study, NO was increased in samples of control patients from T1 (7 days post bleaching), indicating that local inflammation, first detected in the GCF and later in in the saliva samples, was active. Differences between the studies may be due to the nature of the bleaching agents, as the speed of the release of H_2O_2 varies between them.

Despite not affecting pain thresholds, the present data indicate that a red wine rinse is not only safe with regards to bleaching efficacy, but also reduces GCF and salivary NO levels in patients undergoing carbamide peroxide bleaching. Therefore, a wine rinse may be an interesting approach to attenuate bleaching-induced inflammation. This hypothesis is supported by previous data indicating that red wine extracts are anti-inflammatory.[14,15]

It is worth mentioning that bleaching was not performed with a reservoir in the tray, and the tray was designed 1-mm beyond the gingival margin. In fact, some clinicians could predict that, without a reservoir, the bleaching gel could be immediately pressed out of the tray toward the gingival margin, causing some gingival irritation. In the same way, the tray protrudes 1-mm beyond the gingival margin and could, therefore, present a danger to the gingival margin. However, recent clinical studies showed that no significant increase in the gingival aggression was observed when the extent of the tray reservoir was evaluated during at-home bleaching.[43-45]

Among the limitations of the study, a very narrow age range was selected in the present study (18 to 30 years old). Thus, the current findings need to be extrapolated to other age groups with caution. Overall, the evidence gathered here indicates that there is no need for patients to refrain from drinking colored beverages such as red wine in order to undergo tooth bleaching. Data also suggest that small amounts of red wine may be beneficial as it reduces bleaching-induced NO-dependent inflammation in the oral cavity.

Conclusion

The consumption of red wine during at-home teeth bleaching does not interfere with bleaching effectiveness or TS. In addition, the results indicate that patient exposure to red wine reduces the production of periodontal inflammatory mediators such as nitric oxide in the oral cavity.

Acknowledgments

The authors thank FGM Dental Products for the donation of the materials used in this investigation. This study was partially supported by the National Council for Scientific and Technological Development (CNPq) under grants 303332/2017-4 and 308286/2019-7 and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001. The authors declare no conflicts of interest.

References

1. de Geus JL, Wambier LM, Kossatz S, Loguercio AD, Reis A. At-home vs in-office bleaching: a systematic review and meta-analysis. Oper Dent 2016;41:341–356.

2. Karadas M, Seven N. The effect of different drinks on tooth color after home bleaching. Eur J Dent 2014;8:249–253.

3. Attia ML, Aguiar FH, Mathias P, Ambrosano GM, Fontes C, Liporoni PC. The effect of coffee solution on tooth color during home bleaching. Am J Dent 2009;22:175–179.

4. Liporoni PCS, Souto CMC, Pazinatto RB, et al. Enamel susceptibility to coffee and red wine staining at different intervals elapsed from bleaching: A photoreflectance spectrophotometry analysis. Photomed Laser Surg 2010;28:S105–S109.

5. Berger SB, Coelho AS, Oliveira VAP, Cavalli V, Giannini M. Enamel susceptibility to red wine staining after 35% hydrogen peroxide bleaching. J Appl Oral Sci 2008;16:201–214.

6. Rezende M, Loguercio AD, Reis A, Kossatz S. Clinical effects of exposure to coffee during at-home vital bleaching. Oper Dent 2013;38:229–236.

7. Chen Y, Yang S, Hong D, Attin T, Yu H. Short-term effects of stain-causing beverages on tooth bleaching: A randomized controlled clinical trial. J Dent 2020;95:103318.

8. Hass V, Carvalhal ST, Lima SNL, et al. Effects of exposure to cola-based soft drink on bleaching effectiveness and tooth sensitivity of in-office bleaching: A blind clinical trial. Clin Cosmet Investig Dent 2019;11:383–392.

9. Matis BA, Matis JI, Wang Y, Monteiro S, Al-Qunaian TA, Millard R. Labeled vs actual concentration of bleaching agents. Oper Dent 2013;38:334–343.

10. Cortes G, Pini NP, Lima DANL, et al. Influence of coffee and red wine on tooth color during and after bleaching. Acta Odontol Scand 2013;71:1475–1480.

11. Biasi F, Deiana M, Guina T, Gamba P, Leonarduzzi G, Poli G. Wine consumption and intestinal redox homeostasis. Redox Biol 2014;18:795–802.

12. Castaldo L, Narváez A, Izzo L, et al. Red wine consumption and cardiovascular health. Molecules 2019;24:3626.

13. Sánchez MC, Ribeiro-Vidal H, Esteban-Fernández A, et al. Antimicrobial activity of red wine and oenological extracts against periodontal pathogens in a validated oral biofilm model. BMC Complement Altern Med 2019;19:145.

14. Tsai SH, Lin-Shiau SY, Lin JK. Suppression of nitric oxide synthase and the down-regulation of the activation of NFkappaB in macrophages by resveratrol. Br J Pharmacol 1999; 126:673–680.

15. Chalons P, Amor S, Courtaut F, et al. Study of potential anti-inflammatory effects of red wine extract and resveratrol through a modulation of Interleukin-1-beta in macrophages. Nutrients 2018;10:1856.

16. Colares VLP, Lima SNL, Sousa NCF, et al. Hydrogen peroxide-based products alter inflammatory and tissue damage-related proteins in the gingival crevicular fluid of healthy volunteers: a randomized trial. Sci Rep 2019;9:3457.

17. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. Int J Surg 2012;10:28–55.

18. International Commission on Illumination. Recommendations on Uniform Color Spaces, Color Difference Equations, Psychometric Color Terms. Supplement 2 to CIE, publication 15. Paris: Bureau Central de la CIE, 1978.

19. Maran BM, Vochikovski L, de Andrade Hortkoff DR, Stanislawczuk R, Loguercio AD, Reis A. Tooth sensitivity with a desensitizing-containing at-home bleaching gel a randomized triple-blind clinical trial. J Dent 2018;72:64–70.

20. Darriba IL, Cabirta Melón P, García Sartal A, Ríos Sousa I, Alonso de la Peña V. Influence of treatment duration on the efficacy of at-home bleaching with daytime application: a randomized clinical trial. Clin Oral Investig 2018;23:3229–3237.

21. Paravina RD, Ghinea R, Herrera LJ, et al. Color difference thresholds in dentistry. J Esthet Restor Dent 2015;27:S1–S9.

22. Ciancarelli MGT, di Massimo C, de Amicis D, Ciancarelli I, Carolei A. Moderate consumption of red wine and human platelet responsiveness. Thromb Res 2011; 128:124–129.

23. Bernardon JK, Sartori N, Ballarin A, Perdigão J, Lopes GC, Baratieri LN. Clinical performance of vital bleaching techniques. Oper Dent 2010;35:3–10.

24. Lima SNL, Ribeiro IS, Grisotto MA, et al. Evaluation of several clinical parameters after bleaching with hydrogen peroxide at different concentrations: A randomized clinical trial. J Dent 2018;68:91–97.

25. Mendes SJF, Sousa FIAB, Pereira DMS, et al. Cinnamaldehyde modulates LPS-induced systemic inflammatory response syndrome through TRPA1-dependent and independent mechanisms. Int Immunopharmacol 2016;34:60–70.

26. Dahl JE, Pallesen U. Tooth bleaching a critical review of the biological aspects. Crit Rev Oral Biol Med 2003;14:292–304.

27. Esteves-Oliveira M, Pasaporti C, Heussen N, Eduardo CP, Lampert F, Apel C. Prevention of toothbrushing abrasion of acid-softened enamel by CO_2 laser irradiation. J Dent 2011;39:604–611.

28. Esteves-Oliveira M, Wollgarten S, Liebegall S, et al. A new laser-processing strategy for improving enamel erosion resistance. J Dent Res 2017;96:1168–1175.

29. Zirk M, Schievelkamp S, Kemnitz E, et al. Evaluation of novel nanoscaled metal fluorides on their ability to remineralize enamel caries lesions. Sci Rep 2019;9:1942.

30. Attin T, Betke H, Schippan F, Wiegand A. Potential of fluoridated carbamide peroxide gels to support post-bleaching enamel re-hardening. J Dent 2007;35:755–759.

31. Justino LM, Tames DR, Demarco FF. In situ and in vitro effects of bleaching with carbamide peroxide on human enamel. Oper Dent 2004;29:219–225.

32. de Arruda AM, dos Santos PH, Sundfeld RH, Berger SB, Briso AL. Effect of hydrogen peroxide at 35% on the morphology of enamel and interference in the de-remineralization process: an in-situ study. Oper Dent 2012;37:518–525.

33. Robbins JW. Biologic considerations. In: Schwartz RS, Summitt JB, Robbins JW, Santos J (eds). Fundamentals of Operative Dentistry: A Contemporary Approach. Chicago: Quintessence Publishing, 1996;III:1–25.

34. de Geus JL, Fernández E, Kossatz S, Loguercio AD, Reis A. Effects of at-home bleaching in smokers: 30-month follow-up. Oper Dent 2017;42:572–580.

35. Haywood VB. Treating sensitivity during tooth whitening. Compen Contin Educ Dent 2005;26:11–20.

36. do Amaral FL, Sasaki RT, da Silva TC, França FM, Flório FM, Basting RT. The effects of home-use and in-office bleaching treatments on calcium and phosphorus concentrations in tooth enamel: An in vivo study. J Am Dent Assoc 2012;143:580–586.

37. Lopes GC, Bonissoni L, Baratieri LN, Vieira LC, Monteiro S Jr. Effect of bleaching agents on the hardness and morphology of enamel. J Esthet Restor Dent 2002;14:24–30.

38. Lewinstein I, Fuhrer N, Churaru N, Cardash H. Effect of different peroxide bleaching regimens and subsequent fluoridation on the hardness of human enamel and dentin. J Prosthet Dent 2004;92:337–342.

39. de Geus JL, Wambier LM, Kossatz S, Loguercio AD, Reis A. At-home vs in-office bleaching: A systematic review and meta-analysis. Oper Dent 2016;41:341–356.

40. Maran BM, Matos TP, de Castro ADS, et al. In-office bleaching with low/medium vs. high concentrate hydrogen peroxide: A systematic review and meta-analysis. J Dent 2020;103:103499.

41. Baldea I, Olteanu DE, Filip AG, et al. Toxicity and efficiency study of plant extracts-based bleaching agents. Clin Oral Investig 2017;21:1315–1326.

42. Basting RT, Amaral FL, França FM, Flório FM. Clinical comparative study of the effectiveness of and tooth sensitivity to 10% and 20% carbamide peroxide home-use and 35% and 38% hydrogen peroxide in-office bleaching materials containing desensitizing agents. Oper Dent 2012;37:464–473.

43. Morgan S, Jum'ah AA, Brunton P. Assessment of efficacy and post-bleaching sensitivity of home bleaching using 10% carbamide peroxide in extended and non-extended bleaching trays. Br Dent J 2015;218:579–582.

44. Martini EC, Favoreto MW, Coppla FM, Loguercio AD, Reis A. Evaluation of reservoirs in bleaching trays for at-home bleaching: a split-mouth single-blind randomized controlled equivalence trial. J Appl Oral Sci 2020;28:e20200332.

45. Martini EC, Favoreto MW, de Andrade HF, Coppla FM, Loguercio AD, Reis A. One-year follow-up evaluation of reservoirs in bleaching trays for at-home bleaching (Epub ahead of print, 1 Jul 2021). J Esthet Restor Dent doi: 10.1111/jerd.12797.

Lucas Lage Menezes

Lucas Lage Menezes PhD student, Programa de Pós Graduação em Odontologia, Universidade Ceuma, Luís, Maranhão, Brazil

Suellen Nogueira Linares Lima PhD student, Programa de Pós Graduação em Odontologia, Universidade Ceuma, São Luís, Maranhão, Brazil

Etevaldo Matos Maia-Filho Professor, Programa de Pós Graduação em Odontologia, Universidade Ceuma, São Luís, Maranhão, Brazil

Elizabeth Soares Fernandes Professor, Instituto de Pesquisa Pelé Pequeno Príncipe, Curitiba – PR, Brazil

Saulo Jose Figueredo Mendes MS student, Programa de Pós Graduação em Microbiologia, Universidade Ceuma, São Luís, Maranhão, Brazil

Leticia Machado Gonçalves Professor, Departamento Odontologia I, Universidade Federal do Maranhão, São Luís, Maranhão, Brazil

Matheus Coelho Bandeca Professor, Programa de Pós Graduação em Odontologia, Universidade Ceuma, São Luís, Maranhão, Brazil

Alessandra Reis Professor, Programa de Pós Graduação em Odontologia, Universidade Estadual Ponta Grossa, Uvaranas, Ponta Grossa, Paraná, Brazil

Alessandro Dourado Loguercio Professor, Programa de Pós Graduação em Odontologia, Universidade Estadual Ponta Grossa, Uvaranas, Ponta Grossa, Paraná, Brazil

Rudys Rodolfo De Jesus Tavarez Professor, Programa de Pós Graduação em Odontologia, Universidade Ceuma, São Luís, Maranhão, Brazil

Correspondence: Prof Dr Alessandro D. Loguercio, School of Dentistry, Dept REstorative Dentistry, State University of Ponta Grossa. Rua Carlos Cavalcanti, 4748 Bloco M, Sala 64-A, Uvaranas, Ponta Grossa, Paraná, Brazil 84030-900. Email: aloguercio@hotmail.com